AUTHOR INDEX

Akman, S. 359
Andrews, J. S. 267
Aw, T. Y. 61

Ballet, F. 281
Baron, J. 41?
Bertino, J. R. 1
Breakefield, X. O. 391
Brown, J. M. 117
Brown, N. C. 447
Bump, E. A. 117
Chu, F. F. 357
Costall, B. 181

Davis, M. 147
Doroshow, J. H. 359

Esworthy, S. 359

Haahsma, E. E. J. 73
Hart, J. E. 203
Hoyt, D. G. 347
Hsu, Y.-P. P. 391
Huxtable, R. J. 371

Joenje, H. 219
Jones, D. P. 61

Keizer, H. G. 219

Lazo, J. S. 347
Leonard, B. E. 21
Leurs, R. 73
Lockridge, O. 35

Mini, E. 1
Murray, K. J. 329

Naylor, R. J. 181
Nutt, D. J. 233

Patel, J. M. 137
Peters, W. 499
Pinedo, H. M. 219
Pitt, B. R. 347

Ruslum, Y. M. 1

Schuurhuis, G. J. 219
Sebti, S. M. 347
Shan, X. 61
Stephens, D. N. 267

Talanian, R. V. 105
Timmerman, H. 73
Trave, F. 1
Tyers, M. B. 181

Van Riezen, H. 21
Voight, J. M. 419
Vellucci, S. V. 167

Weyler, W. 391
Wright, G. E. 105

SUBJECT INDEX

Adenylate cyclase 330, 331
Adrenergic agonists, hepatic circulation 290–5
Adriamycin *see Doxorubicin*
Alcoholic liver disease, hepatic circulation 306, 307
AMP, cyclic
  compartments 339, 340
  contractile apparatus 336, 337
  metabolism enzymes 330
  phosphodiesterase inhibitors 333, 334
  receptor agonists 332, 333
  smooth muscle, agents increasing 331, 332
  vasodilation mechanisms 329–41
AMP, cyclic; dependent protein kinase 331
AMP derivatives, smooth muscle 334, 335
Amygdala
  anxiety and fear 159, 160
  fear and stimulation 160
Anticancer quinones
  cytotoxicity and glutathione 359–66
  oxygen radical production 359–61
Antimalarial drug resistance
  development 499, 500
  drug pairs 500–5
  multiple drugs 505, 506
  prevention 499–506
    methods 506
Anxiety
  adrenoceptor challenge 242, 243
  amygdala role 159–61
  caffeine effects 237
  diagnosis 234
  drug discrimination 267–77
  drug withdrawal 245
  GABA-receptor drugs 238–40
  peptides 246
  pharmacology 233–52
  provocation by drugs 235–46
  psychiatry 234
  respiratory manipulation 241, 242
  serotonergic agonists 243, 244
  sodium lactate 240, 241
  symptoms 235
  treatment 234, 246–51
    antidepressants 245, 249
    α-adrenoceptors 250, 251
    β-blockers 250
    benzodiazepines 246, 247
    monoamine oxidase inhibitors 249, 250
    new anxiolytics 247, 248
Anxiogenic drugs and behavior 172–6
Anxiolytic drugs and behavior 172–6
Aphidicolin
  derivatives 479–81
  structure 479
Aryl hydrocarbon hydroxylase, lung 419–40

Behavior, olfactory bulbectomy 25–7
  antidepressants 29, 30
Benzo[a]pyrene hydroxylase
  activity in lung 435, 436
  bronchial and bronchiolar walls 435
  histochemistry 429, 430
  3-methylcholanthrene effects 436–8
Bleomycin
  analogs 348
  discovery 347
  metabolism 351–3
  pulmonary fibrosis 347–56
  pulmonary toxicity 348, 349
  structure 348

Calcium vasodilation 337–9
Cholinesterase (*see also* Serine esterase)
  atypical
    gene 53–6
    nucleotide alteration 55
    purification 53
  definition 36, 37
  drugs hydrolyzed 42–4
  gene 52, 53
  genetic variants 38, 39
    ethnic distribution 39
  inhibitors 54, 55
  K variant 56
  phenotyping 41, 42
  silent 56
  succinylcholine fate 37
Cholinesterase protein
  amino acid sequence 48
  contamination 47
  properties 45–50
  purification 46
  subunits 49, 50
Cirrhosis
  hepatic function 304–6
  hepatic microcirculation 300–6
    portal hypertension 302–4
    resistance 301, 302
    scheme 305
Conditioned emotional response (CER)
  amphetamines 145, 154
  barbiturates 153
  benzodiazepines 149, 152, 153
  drugs affecting 150, 151
  ethanol 149
  scheme 148
Conditioned suppression 148, 149
Cyclophosphamide 137–44
  detoxification 138
  lipid peroxidation 142–4
  lung toxicity 144
  membrane fluidity 141, 142
  metabolic activation 138
  metabolism 139, 140
  microsomal membranes 141
  properties 137, 138

Depression
  drug discrimination 267–77

drugs producing 177, 178
separation model 177
DNA analogs
acyclonucleotides 473–7
structure 474, 475
arabinonucleotides 464–9
2′-deoxyribonucleotide 5′-triphosphate derivatives 453
base pairing specificity 459, 460
structures 454–8
2′-deoxyribonucleotide mimics 479–85
structures 479
2′,3′-dideoxyribonucleotides 469–73
structures 469
DNA polymerase effects 447, 448
N^2-substituted 2-aminopurines 484, 485
structures 485
N^6-substituted 6-aminopurines 481–4
structures 482, 483
sugar modifications 462–79
structures 463, 465, 467, 469, 473–5
triphosphate group modifications 477, 478
structures 478
DNA polymerase
analogs 447–89
asymmetric dimer 109, 110
characteristics 449–53
diversity 450
nDNA replication 105–11
inhibition mechanisms 486
inhibitor selectivity 487, 488
inhibitory analog 451
dNTP analog response 487
dNTP derivatives 485
PCNA sensitivity 108, 111
α-role 106, 107
β-role 106
δ-role 107
cofactor 108
properties 107, 108
scheme of reactions 452
yeast DNA replication 110
Doxorubicin cytotoxicity mechanisms 219–28
cardiotoxicity 226, 227
DNA damage and redox cycling 220, 221
free-radical dependent 220
free-radical independent 227, 228
free-radical role 223–7
–iron complex 224
iron complex 222, 224
DNA damage 222
lipid peroxidation 221, 222
metabolism and intermediates 221
radical scavengers 225, 226
Drug discrimination models
antidepressant cue 276
anxiety and depression 267–77
anxiogenic cues 273–6
anxiolytic cue 268–72
benzodiazepine cues 268, 269
excitatory amino acids 272
F67142 cue 275, 276
GABA-B_2 ligands 269–71
pentylene tetrazole cue 273–5
serotonin cue 271, 272
Drug metabolism
and cholinesterase 42–4
esterases 45
Drug pairs in malaria 500–5
blood stage effects 504
life cycle stages 502–4
potentiating 500–2
Drug resistance, antimalarial 499–506

Estrogen
adrenal effects 209, 210
blood and bone marrow effects 211, 212
blood and bone pathology 207, 208
endocrine pathology 203–15
growth 208, 211, 212
liver effects 208, 209
liver and kidney pathology 205–7
pituitary effects 209, 210
reproductive pathology 204, 205
role 203
toxicity 204
effects 213
uterus effects 210, 211

Fear and amygdala role 159–61
Fear-potentiated startle effect 154–9
acoustic 158
amygdala role 158, 159
drug effects 155–7
fear anxiety study 155
features 155
neural systems 157
5-Fluorouracil (5-FU)
antitumor activity and folinic acid 1–14
experimental models 3–7
mechanism of action 2, 3
metabolism 2
Folate enzymes 3
Folinic acid (LV_1, leucovorin)
clinical trials 7–14
breast cancer 12
colorectal cancer 10, 13
gastric cancer 12
head and neck cancer 11
lung cancer 12
5-FU antitumor enhancement 1–14
in vitro tumor systems 3–6
in vivo models 6, 7
leukemia cell growth 3
pharmacokinetics 7–9
tumor pharmacology 8, 9

Gene, cholinesterase 52, 53
atypical 53–6
Glutathione
aging 67, 68
degenerative disease 67, 68
free radical protection 64
functions and radical-induced injury 63, 64
homeostasis 61–3
ischemia–reperfusion injury 64, 65
lipid peroxidation 66, 67
radiation damage 65, 66
radioprotection 117–32
synthesis and oxygen 62
Glutathione–glutathione peroxidase cycle 362, 363
antitumor activity 363, 364
cardiac toxicity 364–6
quinone toxicity 359–66
tumor cell resistance 364
Hepatic circulation 281–317
adrenergic agonists 290–5
alcoholic liver disease 306, 307

blood volume 297
cirrhosis 300–6
disease 299–317
endothelial cells 286, 287
experimental injury 308–16
carbon tetrachloride 315, 316
chemical 315
endotoxin 311–13
hypothermia 309
hypoxia 308–11
ischemia 308–11
necrosis 313, 314
virus 314
fat-storing cells 287, 288
fluid exchanges 297–9
Kupffer cells 287
microcirculation 284, 285
microvasculature and metabolism 299, 300
nerves 282, 283
organization 282, 283
physiology 288–99
platelet-activating factor 295
pressure–flow curve 289
resistance, regulation 290
sinusoid structure 285–8
space of Disse 288
structure 282–8
sympathetic nerves 295

Membrane structure 141
Midazolam, monkey behavior 174–6
Monkeys
β-CCE effects 172, 173
midazolam and dominance 174–6
Monoamine oxidase 391–408
aging 405
amino acid sequences 401
assay methods 395, 396
biosynthesis 398, 399
catalytic cycle 391
chemical mechanism 397, 398
development 403, 404
disease role 406–8
distribution 392–4
electrophoresis 393
genes 399
hormone effects 405, 406
inhibitors 395
kinetic mechanism 396, 397
lipid interaction 394
molecular genetics 401–3
regulation 403–6
substrates 394, 395
subunit structures 396
Monoamine oxidase A genes 400
Monoamine oxidase B genes 399, 400

Olfactory bulbectomy
behavior changes 25–7
antidepressants 29, 30
tests used 26–9
neuroanatomical connections 23–5
neurotransmitter changes 29, 30
procedure 22, 23
psychotropic drug effects 21–31
rodent strain effects 25
weight 22, 23
Oxidative injury, glutathione-dependent protection 61–8
Oxygen radical toxicity sites 361, 362

Panic
noradrenergic dysfunction 252
routes to 236
Psychotropic drugs, olfactory bulbectomy 21–31
Pulmonary fibrosis
bleomycin 347–56
bleomycin-induced 349
animals 349–51
DNA integrity 353, 354
lipid effects 354
mechanisms 353
prevention 355
RNA effects 354, 355
changes 348
Pulmonary toxicity, pyrrolizidine alkaloids 371–85
Pyrrolizidine alkaloids
angiotensin-converting enzyme 379
cardiopulmonary toxicity 373–5
dose relationships 381
endothelial changes 377, 378
inflammation 378, 380
lung changes 375–7
occurrence 372
platelet effects 378
pulmonary actions 380, 381
pulmonary toxicity 371–85
structure 372, 373
toxicity modification 382, 383
toxic metabolite 383–5

Radiation
cytotoxicity mechanisms 118–21
DNA 119, 120
lipid peroxidase 121
membrane damage 120, 121
survival curve 118, 119
Radiation response, glutathione role 65, 66, 117–32
aerobic cell 128
hypoxia 126–8
K curves 126
kinetics 125, 126
Radiation therapy
glutathione 129–32
glutathione depletion 129–31
tumor hypoxia 129
Radioprotection, glutathione 117–31
competition model 123, 125
damaged molecule restoration 123, 124
mechanisms 118
off scavenging 121, 122
oxygen depletion 124, 125
peroxyl reduction 124
radical scavenging 122, 123
Radiosensitizers efficacy and glutathione level 131, 132
Receptor, adreno and anxiety 242, 243
Receptor, benzodiazepine and anxiety 245
Receptor, GABA-benzodiazepine model 269
Receptors, histamine 73–99
estrogen activity 98
types 98
Receptors, histamine H_1
analog effects 93
autoradiography 82
calcium influx 80
G-protein regulation 78, 79
in vivo tests 83, 84
ligands and activity 74, 75

agonists 74
antagonists 75–7
formula 75
stereoselectivity 77
mechanism 77, 78
pharmacological models 80
phosphatidylinositol breakdown 78–80
radioligand structure 81
species differences 84
Receptors, histamine H_2
agonist structure 85, 86
chiral compounds 88
analog effects 93
antagonist structures 86, 87
desensitization 92
functionality tests 90, 91
in vivo tests 91, 92
mechanism 88
model, shuttle 89, 90
stereoselectivity 87
subtypes 92
Receptor, histamine H_3
analog effects 93, 94
ligands 95, 96
localization 96
presynaptic 93
role 96, 97
Receptors, 5-hydroxytryptamine$_3$, 5-HT_3
agonist and antagonist effects 198
agonist site of action 190
antagonist site of action 190
anxiolytic antagonists 187–90
aversive behavior 187–91
brain, identification 196–9
fluphenazine effects 184, 185
GR38032
alcohol consumption 196
antagonism 183–6
brain binding 199
locomotor hyperactivity 186
mesolimbic dopamine function 182, 183
psychopharmacology 181–99
withdrawal 191–6
anxiolytics 194–6
diazepam 192
ethanol 192, 193
sites of action 193, 194

Separation models, monkeys 176
Serine esterases, family 50, 51
Social behavior, primate
dominance 168, 169
features 167, 168
macaques 170
squirrel monkeys 170
talapoin monkeys 169
vervet monkeys 170
Stress-induced reproductive suppression 171
Succinylcholine
apnea 37
and dose 39, 40
atypical cholinesterase 36

Vasodilation
AMP, cyclic 329–41
protein kinase 335
calcium levels 337–9
mechanisms 335–9
protein phosphorylation 335, 336

Xenobiotic-metabolizing enzymes
alveolar walls 430–5
bronchial walls 430–5
features 420–3
immunohistochemistry 426–9
preparation 427
staining 428, 429
lung 419–40
3-methylcholanthrene effects 436–8
pulmonary localization 423–9